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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,924	09/12/2003	Paul P. Latta	LATTA.002A	7335

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,924	LATTA, PAUL P.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 05/02/05 is acknowledged.

Claims 2-9 are pending.

Claims 2-9 are under consideration in the instant application.

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

Applicant's arguments, filed 05/02/05 have been fully considered, but have not been found convincing.

Applicant asserts that the title accurately reflects the claimed invention.

Contrary to Applicant's assertion, it is noted that the amended claims of the instant application reads on a method of preventing onset of Type I diabetes. The current title of the application reads on prevention of any type of diabetes.

3. The rejection of: (i) claims 2-5 and 7-9 under 35 U.S.C. 102(e) as being anticipated by US Patent 6,703,017 or by US Patent 5,425764 and (ii) claims 2-9 under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,703,017 or by US Patent 5,425764 each and in view of US Patent 5,529,914 are hereby withdrawn in view of the amendment to claim 1. However, said rejections will be re-introduced when the **new matter** (wherein said dose is at least one order of magnitude less that that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes) is deleted from claim 1.

In view of the amendment, filed 05/02/05 the following rejections remain:

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide **enablement** for a method of preventing onset of Type I diabetes in a mammal , comprising implanting a dose of insulin-producing cells encapsulated in a biologically compatible membrane wherein said dose is at least one order of magnitude less that that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes , for the same reasons set forth in the previous Office Action, mailed on 12/16/05.

Applicant's arguments, filed 05/02/05 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) US PTO has previously accepted the predictability of the results of prevention of diabetes in nod mice and allowed US Patent 6,841,152; (ii) Second Declaration by Dr. Scharp under 37 CFR 1.132 states that the NOD mouse is the only animal model for human autoimmune, type I diabetes because it is the only available model reasonable predictive of human disease; (iii) NOD mouse model is the standart animal model for conducting research on type I diabetes and one skill in the art would accept the NOD model as reasonable correlating to the condition in human.

Contrary to Applicant's assertion, it is noted the claims of the issue patent US 6,841,152 recites method of protecting against the development of autoimmune diabetes, not method of preventing. Moreover, it is well settled that whether similar claims have been allowed to others is immaterial. See In re Giolito, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and Ex parte Balzarini 21 USPQ2d 1892, 1897 (BPAI 1991). Moreover, as stated In re Borkowski, 505 F2d 713,718,184 USPQ29,33 (CCPA 1974), "The Paten Office must have the flexibility to reconside and correct prior decisions that may find to have been in error". In a similar context, the court in Fessenden v.Coe, 38 USPQ 516,521 (CADC 1938) stated that '[t]wo wrongs cannot make a right."

With regards to the second declaration of Dr. Scharp under 37 CFR 1.132. The examiner disagree with the statement that NOD mice model is the only rodent model of type I diabetes. Atkinson et al.,(Nature, 1999, V.5, pages 601-604) teach the advantages of BioBreeding rat as a model of type I diabetes (see entire document, page 603 in particular). Moreover, the data presented in the second declaration of Dr. Scharp under 37 CFR 1.132 clearly indicated that using NOD mice as a model, 40% of the treated animals develop diabetes. In other words, even in NOD animal model in 40 % of the animals the onset of diabetes has not been prevented using the claimed method.

With regards to the issue that NOD model correlating with the condition in human.

Atkinson et al. .,(Nature, 1999, V.5, pages 601-604) teach that in addition to certain NOD strain-specific characteristics that distinguish these mice from humans at risk for type I diabetes important genus-specific features distinguish the murine diabetes as well, such as resistance to ketoacidosis or the absence of the murine homolog of HLA-DR molecules on APC. Investigators have not always considered that. Unfortunately, in a genetically heterogeneous human population containing individuals at high risk of type I diabetes development, there is little evidence that many of them would have a comparable set of immune deficiencies that prove as malleable. In NOD mice, type 1 diabetes development is well-choreographed. In contrast, the natural history of type 1 diabetes in human is such that the age of disease onset is extremely broad; symptoms occur at any time from the first years of life to well beyond 50 years of age. It is clear that the genus-unique and strain-specific aspects of diabetes in NOD mice must be fully understand and appreciated if we are to know which therapeutic protocols are reasonable to extrapolate to humans and which are not. Exploitation of the NOD genome for clinical research is yet to be done (see pages 602, 603 and 604 in particular). Moreover, as has been stated in the previous Office Action, the specification only discloses the effects of the implanting of insulin-producing cells on the level of blood glucose using streptozotocin-induced diabeties in murine experimental model. (See Examples 1-2 in particular). Examples 3-7 in the instant Specification are prophetic examples that indicate what the inventor thinks might happen in the experiments which have not actually been performed. The specification does not adequately teach how to effectively prevent onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane. Knip M (Acta Pediatr. Suppl., 1998, V.452, pages 54-62) teaches that currently the state of the art is that successful prevention of type I diabetes has at least two precondition. First, one must be able to identify individuals at increase risk for progression to type I diabetes and second, must have an intervention modality with less severe adverse effects than those associated with disease itself. Total eradication of clinical type I diabetes cannot be expected in the next century, as it is probable that a combination of different interventions will be needed to achieve an optimal effect (see entire document, page 60 in particular). Mestas et al (J. of Immunology, 2004, 172, pages 2731-238) teach that there exist significant differences between mice and humans in immune system development, activating and response to challenge in both the innate and adaptive arms. As therapies for human diseases become ever more sophisticated and specifically targeted it becomes increasing important to understand the potential limitations of extrapolating data from mice to humans. The literature is littered with the examples of therapies that work well in mice but fail to provide similar efficacy in humans. Teuveson et al., (Immun. Review 1993, N136, pages 101-107) teach that one problem with rodent models of transplantation is that rejection is easily overcome in said models in comparison to the difficulty of overcoming allograft rejection in human (see page 100 in particular). Teuveson et al., further teach that " however today's small animal models seem to be insufficient to produce data for clinical decision-making" and further raises doubt as to whether large animal models can be applied to clinical situations, due to species-specific reactions to treatment (see page 101 in particular). Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there

are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail *in vivo*.

Substantiating evidence may be in the form of animal tests, which constitute recognized screening procedures with clear relevance to efficacy in humans. See Ex parte Krepelka, 231 USPQ 746 (Board of Patent Appeals and Interferences 1986) and cases cited therein. Ex parte Maas, 9 USPQ2d 1746. However, as has been discussed supra, the state of the art is that it is unpredictable form the *in vivo* murine data using NOD model disclosed in the specification as whether the instant invention can be used for the *in vivo* preventing onset of type I diabetes in mammals including human. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of preventing onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane. Thus in the absence of working examples or detailed guidance in the specification, the intended uses of the claimed method of preventing onset of Type I diabetes in any mammal, including human are fraught with uncertainties.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of preventing onset of type I diabetes in mammal predisposed to type I diabetes , comprising implanting insulin-producing cells encapsulated in a biologically-compatible membrane in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

The following new ground of rejection is necessitated by the amendment filed 05/02/05

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 2-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" ... wherein said dose is at least one order of magnitude less that that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes" claimed in claim 1 represent a departure from the specification. The passages pointed by the applicant do not provide a clear support for the " ...wherein said dose is at least one order of magnitude less that that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes. The specification and the claims as originally field only support administering a tolerizing dose of insulin-producing cells encapsulated in a biologically-compatible membrane. The passage pointed by Applicant only generally disclosed that curative dose is between one and two orders of magnitude greater than the tolerizing dose.

7. No claim is allowed

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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